Original Articles.

BERIBERI IN BRAZIL.

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HAVING occasion to visit all of the principal cities of Brazil twice during the past year, I embraced the opportunity to collect such facts as were accessible concerning this strange disease, which, of late, seems to have embraced the whole Atlantic coast of Brazil from 5° north of the equator to 28° south. We have no assurance that it may not yet invade our Gulf coast, where there is a considerable strip of country within the limits ascribed to it, and where conditions apparently favorable to its development exist.

I was shown every courtesy by resident physicians of public or private hospitals, and officials in charge of penal institutions. It was, however, extremely difficult to get statistics of mortality of beriberi, or the extent to which it prevailed; the epidemic was always just in advance, and I never came up with it. There exists a great deal of confusion in the minds of many physicians as to exactly what constitutes a case of beriberi, but in some places, as was observed in the early days of the disease in India, there is a tendency to call every fatal disease of debility or obscure case of dropsy or paralysis, beriberi, so that it is impossible to reconcile statements made concerning it at different points on the coast. I have, therefore, shaken together the results of all of the observations made in upwards of one hundred cases at Para, Maranham, Pernambuco, Bahia, and Rio de Janeiro, and endeavored to give a fair general view.

It is by no means as new in South America as is generally supposed. The first recorded observation of the disease is found in an old Portuguese work of 1756 (1),[1] where it is described as seen in Maranham, in the first half of the last century. Nothing is heard of it for one hundred years or more, when it is again recognized in Bahia (1860). It is probable, however, that it existed in Maranham and the neighborhood from the time of its first settlement, unrecognized, and treated as rheumatism, scurvy, or some of the ordinary medullary and cardio-hepatic diseases. It is also certain that it existed in Bahia many years before the epidemic of 1863 (2). At this time, however, it attracted the attention of observing physicians of the place, among whom were Drs. Patterson, Wurcheron, and Silva Lima, the latter writing and publishing, in 1872 (3), an elaborate description of its clinical features, based upon one hundred and twelve cases, and a review of the literature of the subject, making it clear that the disease was the veritable beriberi of India. It is to be regretted that this eminent clinician has not revised his work of fifteen years ago, and given to the profession the results of his later observations and riper experience, and of the extensive pathological research he is known to have made during this time. With his unrivalled opportunities and his acknowledged ability, no one could make a more valuable contribution to the literature of this obscure subject.

The geographical limits of the disease are now enlarged to include various points of India, the Malabar coast, part of Ceylon, Java, a limited area in Africa, China, and the coast of Bengal, Borneo, Cuba, Paraguay, and Brazil. It has a remarkable tendency to select certain strips of coast, leaving others in the same latitude, and apparently in the same condition untouched. Thus it is found in Java, while at Baly (Clapham), separated only by a narrow strait, it is unknown. In Cuba it has never been recognized out of Cardenas. It occupies the whole coast north of Madras (Lat. 13° 6′ N.), but is never seen south of it (Aitken). It is found only on the west side of the Bay of Bengal, from 15° to 20° N. Lat. In India it never extends more than forty (4) to sixty miles from the coast (Morehead), while in South America it has been seen in Matto Grosso (Araujo Braga), five hundred miles from the coast, and fifteen hundred miles up the Amazon (Herndon), and in São Paulo, at an elevation of nearly three thousand feet (Bertoldi), and in Bolivia, on the Atlantic slope of the Andes. It has been seen as far north as 40° Lat., and as far south as the 28th parallel, though it may be said to be limited to about 25° either side of the Equator. It is a singular fact that the disease has not yet been found in the West Indies, except at Cardenas, in Cuba, nor on the west coast of Africa, nor north coast of South America, nor in any part of Central America or Mexico, or the United States (5).

The very name is suggestive of something foreign, and we are prepared to learn that it is of Indian origin. Its etymology is obscure. It is probably from the Singhalese word *beri*, meaning weakness, inability — equivalent to our generic term *disease*. The repetition is common in the East to indicate intensity. It has also been said to come from the Hindoostanee word *bheri*, a sheep, from the resemblance of the doubling gait of the beriberic patient to the walk of a sheep. Others trace it to bhebheri, meaning numbness, rheumatism, a sore or swelling.

The word was found in use on the Malabar coast, where the disease was first discovered, and has been handed down by Anglo-Indian and Dutch medical writers, as a name for almost every fatal disease of debility, such as various kinds of paralysis, reflex paraphlegia, dropsy, anasarca, scurvy, anæmic rheumatism, various heart diseases, etc., known in the East. Later writers, however, have used it with greater precision. It is known in Japan as kake-kake (6); in Ceylon, as the bad-disease. The "Parangi" — which depopulated the "Vanni" district in Ceylon, and reduced it to a jungle, was probably *beriberi* (Evezard and Clapham). In Africa, it is the *sleeping sickness*. Authors speak of it as *Hydrops Asthmaticus*, *Indosynclonus*, *Synclonus-Beriberia*, etc., etc. So much for the name.

The disease, as found on the Brazilian coast, may be defined as "a constitutional disease, characterized by dropsy, paralysis, degeneration of muscular tissue, and progressive anæmia, whose chief features are numbness of surface, and hyperæsthesia of deep muscles of the extremities — gradual and incomplete ascending paralysis, both motor and sensory. Total absence of fever. Præcordial oppression, scanty and high-colored urine, hoarseness, and dusky discoloration of the skin, the fatal cases terminating by suffocation, asphyxia, or asthenia; favorable cases by an abundant flow of urine (Silva Lima), slow convalescence, and great tendency to relapse (Lacerda)."

Clinically, it may be divided into three forms: 1. The *paralytic*, dry, or atrophic form — *B. Atrophia* — where paralysis is the marked feature, and where there is a deficiency of fluids in the vessels, with, in rare cases, muscular atrophy. 2 The *œdematous* or wet

[1] These figures refer to the Biblography at the close of the article.

form — *B. Hydrops* — in which there is a watery condition of the blood, with effusions into the cellular tissue and serous cavities. 3. The *mixed* — *B. Polysarcia* — where symptoms of either or both the other forms are found, with wide variations, and where the sharp lines of difference are lost.

There are two well-marked stages: the prodromic and the active. There is, in the first, a tired feeling, indisposition to move, weakness about the legs; in walking, a slight inclination of the toes to drag, obliging the patient to step higher than usual, inability to retain on the foot the heelless slipper usually worn by the poorer classes of Brazil; a drowsy feeling, and a sense of extreme shortness of breath on the slightest exertion, loss of appetite, and a sense of fullness at pit of the stomach; slight pains, generally attributed to rheumatism or neuralgia; numbness and tingling at tips of fingers, and of toes, around corners of mouth, and over anterior tibial muscles, a sensation around the waist as of a cord drawn tightly, with a knot over the epigastrium, and a slight pain at or beneath lower end of sternum. Up to this point, the symptoms are common to all forms of the disease. In the *paralytic* form, the patient now begins to feel anxious, the skin of the legs becomes dry and falls *asleep;* there is great sensitiveness, on pressure, about the deeper muscles of the calves of the legs, the belt gets tighter, and the knot over the epigastrium larger and harder, and distresses the patient fearfully, the tightness sometimes reaching up to the axilla, the dyspnœa becomes frightful, the face assumes a livid hue, the pulse becomes small and weak, the urine scanty and almost the color of coffee, the appetite lost; sometimes there are partial convulsions, clonic spasm of the muscles; patient complains that he is suffocating, is covered with cold, clammy sweat, and does really die of suffocation, in full possession of his mental powers, and *without* fever.

In the second form, the dyspnœa is a troublesome symptom and very early there is an unaccountable sense of weariness (canceira); there is an apparent swelling and hardening of the calves of the legs, which is, however, only a contraction of the surrounding tissue; the tendon reflexes are usually exaggerated, rheumatic pains in, and heaviness of the feet, the anasarca, a pathognomonic symptom of this form, first appears in the anterior part of the leg, and *not in the feet,* as in other diseases. The pulse is full and compressible, a systolic murmur is heard over the pulmonary valves, and in the large arteries; the patients become low spirited and alarmed. The dense, and slightly elastic œdema increases everywhere, hardly pitting at all on pressure. The serous cavities fill with effused liquid. There is a slight degree of numbness and often a little paralysis; the urine is, as in the first form, scanty and high-colored, of acid reaction and spec. grav. 1007-1030. Death comes by asphyxia, visceral congestion, or occasionally, by embolism of pulmonary artery (Silva Lima), and sometimes suddenly and unexpectedly (Lacerda).

The symptoms of the third form vary greatly. Sometimes the paralytic, and sometimes the œdematous predominating, and sometimes both come on simultaneously. These are the cases that become suddenly bad, and are known as "*Gallopante*" galloping, or acute pernicious form, the patient dying in six to twenty-four hours. In the mixed form, the sensitiveness of the muscles is very great, the feeling of exhaustion very pronounced; the dyspnœa great, swiftly progressing to asphyxia; there is a rapidly ascending paralysis, involving all of the respiratory muscles. The paralysis, either motor or sensory, is never complete. The sphincters are never involved in either form. There is never œdema without some paralysis, nor a case of pure paralysis, without some œdema; the diaphragmatic belt, a characteristic feature of the disease, is always present, but much more marked in the paralytic than the wet form. Rapidly increasing œdema marks the gravity of the case. In all cases there is a peculiar puffiness and lividity of the face, sometimes producing a mottled appearance. The white line produced by drawing the finger across the surface disappears slowly. In the œdematous cases there is an extreme turgidity of superficial vessels, and not infrequently pulsation of the jugulars. There is often tenderness of the periosteum of the long bones, with a peculiar roughness of surface. Digestion is nearly always deranged; dysentery, diarrhœa, and other tropical diseases often complicate it. Urine is *always* scanty, high-colored and contains epithelial cells, and degenerate fat corpuscles, with urate of ammonia, but rarely any albumen. It is to be regretted that no accurate quantitative analysis has been recorded that shows the amount of urea secreted. The skin is dry and harsh. The walk of the beriberic is unique, resembling that of a child learning to walk; the forward movement is nearly normal, the trouble being in recovering the feet. There is also a peculiar hoarseness of the voice in this disease, accompanied by a jerky, sighing breathing. Many of the isolated symptoms might be attributed to other well-known diseases; it is the grouping together, the peculiar association of the separate features that marks this formidable disease as *sui generis.*

In a disease characterized by symptoms so constant and marked, we should naturally expect to find marked anatomical changes, but we are disappointed. There are no constant lesions met with either in the cord, or large organs that cannot be considered secondary; the blood alone shows important morbid changes in the destruction and degeneration of the red disks, and has evidently lost its nutritive and oxygenating properties. The areola tissues of the heart, lungs, brains, and abdominal viscera, are found soaked in serous fluid, with effusion into the cavities; in eighty per cent. of the wet cases the pericardium is found distended with fluid, containing flakes of fibrin. In this variety the heart is found enlarged, softened and flabby, of pale-yellow color, filled with dark blood, sometimes fluid, sometimes clotted; when the latter, the dark clot extending into the pulmonary artery and large venous trunks. The muscular tissue of the heart-walls is always found undergoing fatty degeneration (which according to Ondcnhover, is often the cause of death). The same condition is found in the tissue of the paralyzed voluntary muscles. In the paralytic form the heart is smaller and empty, and the degenerative changes are less marked.

The appearance of the brain and cord is variable: sometimes the medullary substance seems harder than normal, oftener, however, it is softened. It is frequently found, with ecchymotic spots at emergence of the nerves, the meninges are injected; the cord is sometimes altered by minute effusions of fluid into its substance, congestion of its vessels, spots on the surface of the arachnoid; microscopic examinations have

revealed annular sclerosis invading the antero-lateral pillars, with encysted granular masses in different parts of the spinal marrow. Sclerotic patches in the lumbar and dorsal regions of the cord are often found, the nerve tissue is often yellowish white and granular in appearance (Lacerda). Proliferation of interstitial connective tissue in the lateral columns and posterior roots is found. These varying conditions of the cord, however, do not always bear a just relation to its known mechanism in producing the symptoms found. Serous effusion into the minute connective tissue is the only constant change found.

There is evidently, first, a paresis of the cardiac ganglia, rendering the heart weak, and emptying its cavities; rapid degenerative changes follow in the muscular walls; there is a feeble vis-a-tergo and they yield to blood pressure, thereby producing dilatation and tricuspid insufficiency, with the inevitable regurgitation, capillary stasis and dropsy. A vaso-motor paralysis, acting in like manner upon the pulmonary arteries and arterioles, accounts for the murmur. Congestion alone may destroy life by impairing functions,— by sheer physical changes, and the inevitable consequence which want of circulation entails upon the blood;—blood-stasis, and separation of the elements, formation of coagulum, deposit of pigmentary matter, faulty oxygenation, etc.

If we allow ourselves to consider a single symptom or group of symptoms, the diagnosis is somewhat puzzling; but if regarded as a whole, the symptoms and physical signs present a case not easily mistaken. The individual symptoms, or even a group of the symptoms, may be found in rheumatism, myelitis, trichinosis, scurvy, reflex paraplegia, ordinary anasarca, pernicious anemia, and often the bronzed skin of Addison's disease is observed, granular degeneration of the kidneys, the cachetic dropsy of Andral, various forms of heart disease, and almost every disease due to profound anemia; but in all these there is some essential feature lacking, or in beriberi, there are well-marked symptoms incompatible with the known facts in other diseases. It is essentially a disease of inanition; there is starvation of the cerebro-spinal centres, and consequent anemia, from some important change in the blood that impairs the complex process of nutrition.

The pathognomonic features are the gait, fatigue, the diaphragmatic belt, and incomplete ascending paralysis, never involving the sphincters. The anæmia can hardly be said to be a distinguishing feature, as it is the most common of all conditions incident to tropical life.

What can we say of the cause of the disease? We cannot resort to that convenient term, malaria or marshmiasm,—the great asylum of all obscure diseases,—as it has none of the chief characteristics of malaria, no chill no fever, and when epidemic, almost no recoveries. It has a much narrower limit, also, and is not found in many places where malarial disease most abounds. Then, again, when we say malaria, we say nothing precise or definite, and before we use the term in so important a connection, we should at least define it, and give its elements a fixed character, and explain their *modus agendi*. We have only two points to guide us: first, its limited range and erratic distribution; second, the fact that it requires a residence of six or eight months to be subject to it.

One is thoroughly impressed with the belief that it depends upon some specific poison generated outside of the body; this belief finds corroboration in the fact that Dr. J. B. Lacerda, Director of the Government Laboratory of Experimental Physiology in Rio, and the discoverer of the application of permanganate of potash to snake-bites, has actually found in the spinal marrow and blood of persons dying of beriberi, and isolated, a germ which is in some manner constantly related to the disease.

Dr. Lacerda (7) has published a very interesting work, describing the micro-germ, and telling how he discovered it. He also finds the identical germ in certain kinds of rice. This receives strong support from observers in India where rice is one of the articles of diet *prohibited* to beri-beric patients. This talented observer has, during the past year, pushed his studies into a still more interesting field, and has found the microbe of beriberi to be identical with that which produces the horse-pest (*Peste de Cadeiras*) in the great island of Marajo (8). This disease of horses, in its clinical features, so closely resembles beriberi in the human subject, that Dr. Lacerda's discovery causes no surprise. It also receives strong support from the fact that, wherever the pest exists there also beriberi is found; to wit: in Bolivia, on the Solimoes (Herndon) Mattogrosso, Madras, (9) etc.

The limits of this paper oblige me to forego the pleasure of giving a synopsis of this most interesting work of one of Brazil's foremost investigators. Suffice it to say, that he follows Pasteur's methods, and has isolated this germ, which belongs to the great group of *ascomycites*, and cultivated it, and demonstrated its effects upon various animals, and its causal relation to beriberi, in a most convincing manner. If we accept this, the pathology is comparatively simple. The wide diversity of symptoms is explained by the periods of vegetation, or greater or less activity of the germ, as well as the varying susceptibility of persons attacked. The universal law governing the action of these micro-germs also obtains; in order that they may become noxious elements it is necessary that the normal forces of resistance be lowered, or that some inter-current abnormal condition be present, lack of acclimation is simply lack of habit to resist.

The question naturally suggested is, does the poison primarily affect the blood or the nervous system? The first evidence of morbid change is in the nervous system. The pain, an early and a characteristic symptom, depends upon a hyperæmic condition of the affected parts, due to a vaso-motor paralysis. The varying periods of incubation do not imply any difference in the character of the germ, but it is a question of the quantity introduced and the degree of resistance which it meets. The evidence that there is a primary lesion in the cord is strong; the paralysis is due to pressure from effusion; the effusion dependent upon rapid, destructive changes in the blood. The distrophy, the marasmus, would be indirectly connected with the disturbed function of the cord. The œdema would be referred to the disturbance of the vaso-motor enervation.

The slight paralytic disturbance, in the wet form, where trophic changes predominate, only shows how variable is the localization of the medullary trouble, now in the motor region, and again in the trophic area. Admitting the existence of a specific germ, we easily understaud how the pathological changes are most sharply accentuated in the spinal marrow; a se-

lective affinity, which is a property of all morbigenic germs, enables it to seek the spinal marrow, as the most congenial breeding ground.

Once established in the cord, it has a two-fold action, a mechanical and obvious one, blocking up the capillaries, and disturbing the interstitial circulation, producing congestion, compression of the cellular elements, and consequent atrophy; a chemical action produced by the poisonous detritus, or ptomaines of the micro-organism, in its rapid reproductions, with their well-known fermenting and dissolvent action upon the blood, which is the receptacle of all the residue of organic cellular life; and this explains the dyscrasia, and the rapid and general serous transudation, the acute anasarca, which is the gravest feature of the disease. Now, then, it is not difficult to connect the symptoms with the lesions of the cord, as far as observed, and which are located chiefly in the lumbar and dorsal regions. When we remember that the spinal cord more completely fills the vertebral canal in the dorsal region, than either above or below, it will be understood how symptoms from serous effusion and other lesions will manifest themselves, first, by paralysis and unsteadiness of the lower limbs. Again, the nerves which supply the skin and muscles of the leg and foot arise from the third sacral, and are damaged by a lesion involving the lower part of the lumbar enlargement. It will be remembered that one of the earliest symptoms is a pain in the lumbar region. The actual loss of sensation with wasting points, especially if irregularly distributed, as in beriberi, refers to damage of the nerve-roots, outside of the cord, and relates to the meninges rather than the cord. This, too, coincides with observed lesions. (Lacerda.) Subacute and symmetrical myelitis of the anterior cornua, in the lumbar and cervical enlargement, causes paralysis and atrophy of all four extremities, the upper part of the limbs being normal; the sclerotic patches already mentioned, and other changes are most frequently found in this region.

The morbid agent and its products are eliminated slowly through the kidneys.

It is generally supposed that the number of deaths from beriberi is greater than that of any other disease on the Brazilian coast. I am inclined to think that this is an exaggeration. The percentage of deaths among those attacked is very much smaller than it was fifteen years ago, and it would be safe to say does not exceed 30 to 40 per cent.

Dr. Silva Lima's report of 112 cases gives the death-rate as 62.50 per cent. as follows:

Paralytic, 66 cases with 33 deaths . .	50 %	62.50%.
Œdematous, 23 cases with 18 deaths .	78.26 %	
Mixed, 23 cases with 19 deaths . . .	82.60 %	

In India the death-rate is usually about 25 to 30 per cent. (Malcolmson).

The coast line where it prevails in Brazil, is nearly 3,000 miles long, from Manáo's, on the Amazon, to Santa Catherina, and its existence at all seasons of the year enables the aggregate of its victims to reach a high figure (10).

Concerning the treatment: this is extremely simple. Drugs do no good whatever. The patient should be removed at the earliest possible moment to a place where beriberi does not prevail. Bahia, beautifully situated along a high ridge, easily drained and continually exposed to the sea breeze, seems to be the headquarters of the disease. If patients are removed early before irreparable damage has been done, to the island of Itaparica, a low, flat place, just across the bay, they recover almost as if by magic.

The treatment should plainly be directed to removing the effused fluids, regulating the functions of the important abdominal viscera, especially the kidneys, increasing the action of skin and restoring to the blood its normal constituents; to these ends diuretics, cathartics and tonics are indicated. In India, Maxwell gave phosphorus in substance in 1–2–3 grain doses with success (11). (Lacerda explains the predilection of the micro-germ for the nervous tissue by the fact that this tissue abounds in phosphorus and he observed that the microptyte multiplied most rapidly in a culture acidulated with phosphoric acid.) A great variety of medicines are given, but change of surroundings is the only thing that cures, and in the acute pernicious type this fails. In Pernambuco a preparation of the "Mandioca" plant is used, and has a local reputation. It is simply a powerful diuretic. The *treek-farook*, so extensively used in India, is composed chiefly of terbinthinates with rhei and acts as a prompt diuretic and cathartic (12).

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REPORT ON THERAPEUTICS.[1]

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ERGOT.

NOT long ago, Professor Kobert showed that the noteworthy constituents of ergot are ergotinic acid, which does not promote uterine contractions, and cornutine and sphacelinic acid, which do. What he has published in the *Practitioner*[2] will be found of interest.

"Ergotinic acid: As regards this substance and its sodium salt, I may say I have administered it internally and hypodermically to pregnant bitches, rabbits, cats, and sheep. The doses given were at first small, and then increased, till finally they were toxic. The results of all these experiments entirely agreed with my former ones; when administered internally, even the largest doses are well borne, without the supervention of uterine contractions, and without any material disturbance of the mother. At most, the stools became semi-fluid. When injected subcutaneously, relatively large doses cause complete narcosis, lasting twenty-four to forty-eight hours, during which reflex action ceases; nevertheless, neither contraction of the uterus nor expulsion of the young occurs.

"After very large doses the blood-pressure falls very low, and, as a consequence, the young die, but are not expelled. From these experiments, it will be

[1] Concluded from page 279.
[2] Vol. 35, p. 415.